of interest, associated with a second chromosome not responsible for the aneuploidal trait, condition or abnormality not present in the pregnant female, to detect and quantify the level of second marker nucleic acid present in the sample;

determining that the level of first marker nucleic acid in the sample differs from and is greater than the level of second marker nucleic acid; and thereby

identifying the presence in the sample of the specific chromosomal aneuploidal trait, condition or abnormality of fetal origin.

47. The method of claim 46 wherein the chromosomal aneuploidal trait, condition or abnormality is Down's Syndrome.

48. The method of claim 46 wherein the quantification of the level of marker nucleic acid in the maternal serum or plasma is by quantitative polymerase chain reaction. --

REMARKS

Applicants wish to thank the Examiner for the courtesies extended in interviewing applicants' representatives on November 26, 2002.

During that interview applicants proposed the submission of independent claims directed to preferred embodiments of the invention and claims 37-48 are now submitted in this response.

Independent claims 37 and 39 and their dependent claims 38 and 40 are methods for the *qualitative* determination of a fetal genetic trait, condition or

abnormality. Claim 37 specifies use of a primer/probe set specific for nucleic acid of interest, associated with a genetic trait, condition or abnormality not present in the pregnant female. Claim 39 specifies use of a probe specific for the nucleic acid of interest and use of a sample taken from a pregnant female after the seventh week of pregnancy. These claims are supported by disclosures in the specification, *e.g.*, (all references are to the numbered paragraphs in the published specification, US 2001/0051341) at paragraphs 0007 - 0009, 0012, 0022 and Example 1.

Independent claims 41 and 45 and their dependent claims 42-44 are methods for the *quantitative* determination of a fetal genetic trait, condition or abnormality. Claim 41 specifies use of a primer/probe set specific for nucleic acid of interest, associated with a genetic trait, condition or abnormality not present in the pregnant female. Claim 45 specifies use of a probe specific for the nucleic acid of interest and use of a sample taken from a pregnant female after the seventh week of pregnancy. These claims are supported by disclosures in the specification, *e.g.*, (all references are to the numbered paragraphs in the published specification, US 2001/0051341) at paragraphs 0007 - 0009, 0012, 0019, 0022 and Examples 3 and 5.

Independent claim 46 and its dependent claims 47-48 are methods for the *quantitative* determination of an aneuploidal genetic trait, condition or abnormality in a sample taken from a pregnant female after the seventh week of pregnancy. Claim 46 specifies use of two probes, one specific for a chromosomal marker nucleic acid of

interest, associated with a first chromosome responsible for an aneuploidal trait, condition or abnormality, and a second probe specific for a second chromosomal marker nucleic acid of interest, associated with a second chromosome not responsible for the aneuploidy, to determine that the levels of the two markers differ and thereby confirm the presence of the aneuploidy. These claims are supported by disclosures in the specification, *e.g.*, (all references are to the numbered paragraphs in the published specification, US 2001/0051341) at paragraphs 0007 - 0009, 0012, 0018, 0020 and 0022.

The new set of claims submitted herewith have been formulated in accordance with the approaches discussed during the interview and are believed to be presently allowable.

Favorable consideration and allowance of claims 37-48 are respectfully requested.

Respectfully submitted,

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